THE SIGNIFICANCE OF CERTAIN CONTROL SYSTEMS IN DEVELOPING ADAPTATION TO HYPOXIA

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ABSTRACT: We studied the role of the cerebral cortex, the cerebellar cortex, the adrenal cortex and the pituitary in the process of adaptation of an organism to a moderate degree of hypoxia. It was shown that removing the cortex of one and two of the major hemispheres will lead to a significant increase in the tolerance of animals to acute hypoxia, in which case the adaptation of such animals to moderate hypoxia will exert no substantial influence on altitude tolerance.

Removal of the cerebellar cortex reduces the tolerance of animals to acute hypoxia. After adaptation of the animals to hypoxia the removal of the adrenal cortex is not accompanied by a complete disappearance of the adaptation effect- the altitude tolerance remains higher than in the intact animals.

In spite of the fact that the problem of acclimatization to /137
high altitude conditions has attracted the attention of physicians, physiologists and biologists for more than 100 years, the physiological mechanisms responsible for this process are still to a large degree unexplained.

The development of adaptation to hypoxia (the basic factor of high altitude) results in a reconstruction of the control systems of an organism at various levels. In this respect it is of definite interest to explain the significance for the formation of adaptation to hypoxia of several of the most important regulators, under normal life conditions, which determine integration of the various functional systems. The proposed research was devoted to a study of this question. We investigated the role of the cerebral cortex, the cerebellar cortex, the adrenal cortex and the pituitary in the formation of the process of adaptation to hypoxia.

The experiments were carried out on white rats in conjunction with N.A. Roshchinaya, V.K. Martens, I.D. Bogachevaya and A.V. Shchedronovaya.

In the different series of experiments we used sexually mature males and females with a weight of 100-200 grams. Adaptation of the animals to hypoxia was accomplished both under natural condi-

tions, i.e., in the Caucasus in the region of Mt. Elbrus at altitudes of 2000 and 4000 m, and 3000-5500 m with continuous residence of the animals at these altitudes for a period of 20-30 days; we also carried out an interrupted "adaptation" in which the animals /138 remained daily for a period of 6 hours with continuously increasing altitudes from 3500-7000 m.

In the experimental animals, in the process of adaptation and at the end, we determined the amount of hemoglobin, erythrocytes and reticulocytes in the peripheral blood, we measured according to the Kalabukhov method the oxygen requirement and established by gradual ascent in a pressure chamber the altitude ceiling, i.e., the tolerance to acute hypoxia.

A relatively small amount of research has been devoted to studying the role of the cerebral cortex in the process of adaptation to hypoxia. Arkhangel'skaya noted that the removal in white rats of parts of the cortex results in a slight increase in tolerance to acute hypoxia [1], A.G. Filatova after complete removal of the cortex in pigeons also noted a small increase in tolerance [8]. Thus in these research projects it was shown that the removal from the animals of such an important regulator as the cortex does not result in a lowering of tolerance to hypoxia but unexpectedly even promotes an increase in tolerance of the organism to the effect of acute oxygen deficiency.

We were first of all interested as to whether or not the animals who had the cortex removed in the process of altitude conditioning had an increased tolerance to acute hypoxia; in the literature we have been unable to find any data on this question.

We removed one and two of the hemispheres in 45 animals. Twelve mice with one hemisphere removed, 12 with completely removed hemispheres and 10 intact animals were subjected to adaptation to hypoxia in a pressure chamber at altitudes up to 7000 m. The remaining animals who were operated on and 10 intact animals were kept for control

In the animals who were operated on and in the intact animals the residence under conditions of lowered pressure led to an increase in the blood in the number of erythrocytes, reticulocytes and hemoglobin. Earlier similar results were obtained in the laboratory by Lauer, Kolchinkaya and Turanov in experiments on dogs.

Unlike the intact animals in the rats with one and two hemispheres removed in the process of adaptation no lag in the weight of the body was noted in comparison with the control animals.

A stay at high altitude did not produce in the intact animals any changes in the amount of oxygen requirement.

In the animals who had their cortex removed, after remaining

TABLE 1. TIME OF SURVIVAL OF DIFFERENT GROUPS OF EXPERIMENTAL ANIMALS UNDER CONDITIONS OF ACUTE HYPOXIA

Group	Experimental Animals											$\bar{x}$	σ	m
	1	2	3	4	5	6	7	8	9	10	11			
Intact	3'15"	11'30"	14'	9'	17'	19'20"	16'20"	7'50"	10'40"	11'30"		11'25"	4'9"	1'6"
Intact, Acclimatized	12'45"	16'30"	16'45"	19'30"	22'	24'	21'40"	25'40"	17'30"	9'50"		18'37"	6'2"	2'06"
Without One Hemisphere	5'10"	13'20"	19'	17'20"	17'20"	16'05"	18'20"	20'20"	22'			16'35"	5'1"	1'82"
Without One Hemisphere, Acclimatized	17'	19'55"	19'	18'30"	19'30"	18'	19'	21'	21'	23'	20'30"	19'40"	1'53"	0'49"
Without Two Hemispheres	11'15"	14'30"	14'30"	17'	20'	17'30"	18'30"	24'30"	19'10"	15'20"		17'15"	3'63"	1'21"
Without Two Hemispheres, Acclimatized	12'20"	20'	18'30"	18'30"	25'30"	20'20"	20'10"	25'	26'	20'		20'39"	3'74"	1'24"

TABLE 2. TIME OF SURVIVAL OF DIFFERENT GROUPS OF EXPERIMENTAL ANIMALS UNDER CONDITIONS OF ACUTE HYPOXIA

Group	Experimental Animals										$\bar{x}$	σ	m
	1	2	3	4	5	6	7	8	9	10			
Acclimatized Without Cerebellar Cortex	10'	8'30"	3'20"	12'	14'	5'	11'40"	15'10"			9'57'	3'8"	1'42"
Control Without Cerebellar Cortex	2'20"	15'10"	15'	3'15"	2'10"	5'40"	1'30"	3'05"	2'20"		5'40"	5'27"	1'9"
Acclimatized, Intact	5'45"	3'45"	15'10"	15"	12'	19'10"	7'10"	7'30"	15'20"	10'50"	11'10"	6'18"	2'6"
Control, Intact	10'45"	10'	8'40"	10'50"	15'	7'50"	3'05"	1'20"	14'	2'30"	8'21"	4'76"	1'58"

in a pressure chamber there was noted an insignificant statistically unreliable decrease in the oxygen requirement.

Removal of one and especially of two of the hemispheres led to a significant increase in the tolerance of the animals to acute hypoxia (Table 1). Adaptation of the animals who had their cortex removed to conditions of lowered barometric pressure increases the /140 altitude ceiling relatively insignificantly. However, it nevertheless remains somewhat higher than in the intact animals who were adapted to the same conditions.

Thus in animals after the removal of the cerebral cortex the tolerance of the respiration center to acute hypoxia is significantly increased.

Adaptation of the animals who had the cortex removed to conditions of lowered barometric pressure leads to a further increase in the resistance of the respiration center to hypoxia. In this case removal of one hemisphere produces almost the same increase in resistance of the animals to hypoxia as does the removal of two hemispheres.

Adaptation of the animals with cortex removed leads to a further slight increase in the tolerance of the respiration center to hypoxia. This effect is expressed considerably less than the effect which is caused only by the operational removal of the cortex.

The role of the cerebellar cortex in the process of adaptation of an organism to hypoxia has not been studied sufficiently. There exist only data concerning injury of the cerebellar cortex, its partial removal in puppies and in rats leads to a decrease in altitude tolerance [2].

To explain the role of the cerebellar cortex in the process of adaptation of animals to acute and to chronic oxygen deficiency we carried out experiments in which the cerebellar cortex was removed from the animals after which they were subjected to the effect of lowered barometric pressure. The experimental results showed that after removal of the cerebellar cortex (morphological control permitted establishing that in more than 50% of the animals it was removed completely) there was noted a decrease in the number of erythrocytes and the amount of hemoglobin in the peripheral blood and the animals lagged in weight.

The tolerance of the animals who were operated on to acute hypoxia established according to the time of retention of life of the rats at high altitudes remained lower than in the intact animals (Table 2). A prolonged stay of such animals under conditions of lowered barometric pressure was accompanied by an increase in the erythrocytes, reticulocytes and hemoglobin in the blood and an increase in the altitude ceiling. These data confirm the results of research previously carried out by Barbashovaya. Here no substantial change in the oxygen requirement was noted. The cellular

structures of the cerebellar cortex are quite sensitive to oxygen deficiency with respect to which we might assume that removal of the cerebellar cortex similar to extirpation of the cerebral cortex, may lead to an increase in the tolerance of the organism to acute hypoxia. However, such does not happen. The difference in the appearance of the adaptation effect following removal of the cerebellar cortex and the cerebral cortex apparently is due to the non-identical influence of these formations on the subcutaneous structures and in first order on the respiration center.

In many papers it has been noted that the removal of the adrenal cortex lowers the tolerance of animals to acute hypoxia. The question as to the possibility of developing adaptation to prolonged effect of lowered barometric pressure after removal of the adrenal cortex has been studied very little. In the monograph by Barbashovaya this possibility was negated [2]. /141

Study of the process of adaptation to lowered barometric pressure in animals following removal of the adrenal cortex was carried out both under high-altitude conditions and in a pressure chamber at different altitudes.

In the process of remaining in the mountains, in animals who have undergone adrenalectomy just as in those who are intact there was detected an increase in the erythrocytes, reticulocytes and hemoglobin. No changes in the oxygen requirement here were detected. After returning from the mountains the altitude ceiling in the animals who had under gone adrenalectomy were significantly higher than in the control animals.

The results of experiments carried out in the pressure chamber permitted us to note that the adaptation effect determined from the changes in the blood and the increase in tolerance to acute hypoxia in the animals who had undergone adrenalectomy just as in the intact animals depends on the conditioning schedule under conditions of lowered barometric pressure.

Here it was found that in animals who had undergone adrenalectomy the range of altitudes for which adaptation was possible is lowered. Thus the intact animals are conditioned for prolonged stay at altitudes of 5500-6000 m at which the majority of the animals who had undergone adrenalectomy died.

In a special series of experiments the adrenal cortex in animals was removed directly after adaptation of them to altitude. Setting up the experiment in this way permitted us to obtain information as to whether there does exist "recording of acclimatization" in the adrenal cortex and what significance it has for the appearance of the adaptation effect.

The results of these experiments showed that removal of the adrenal cortex somewhat lowers the adaptation effect (altitude

TABLE 3. SURVIVAL TIME OF ANIMALS UNDER CONDITIONS OF ACUTE HYPOXIA

Group	Experimental Animals												$\bar{x}$	σ	m
	1	2	3	4	5	6	7	8	9	10	11	12			
Intact	11'20"	13'10"	11'05"	4'20"	17'15"	9'20"	8'	5'40"	13'10"	3'35"	16'05"		10'18"	4'65"	1'4"
Intact Acclimatized	15'25"	17'40"	8'10"	16'55"	17'05"	11'40"	13'	13'45"	18'10"	17'			14'53"	3'16"	1'05"
Adrenalectomized	4'	18'10"	8'20"	14'30"	12'30"	13'	5'50"	6'05"	5'	12'04"	10'30"	11'50"	10'09"	4'36"	1'3"
Adrenalectomized, "Acclimatized"	9'15"	15'	11'30"	13'40"	17'30"	18'20"	12'30"	12'30"	11'30"	12'30"	10'30"		13'09"	3'6"	1'14"

ceiling and changes in blood). However, it does not completely remove it (Table 3).

Thus, analysis of the experimental data permits us to conclude that removal of the adrenal cortex does not exclude the possibility of adapting animals to conditions of moderate degrees of atmospheric evacuation. Here in animals who have undergone adrenalectomy there is noted an increase in their tolerance to acute hypoxia and it is of such a nature as in the intact animals' changes in the blood.

Study of the adaptation to conditions of lowered barometric pressure in the mountains at altitudes of 2000 and 3800 m in animals who have undergone hypophysectomy showed that removal of the pituitary leads to a drop in the level of the hemoglobin, the number of erythrocytes and reticulocytes in the peripheral blood.

However, in spite of the lack of adaptation reactions, from the side of the blood, the tolerance to acute hypoxia after remaining in the mountains in animals who have undergone hypophysectomy is increased.

This research has shown that the removal of the most important regulators of the organism by operation (cerebral cortex, cerebellar cortex, adrenal cortex, pituitary) does not excluded the possibility of adaptation of an organism to lowered barometric pressure although it changes its course.

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